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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/051,956	01/16/2002	Larry Mobraaten	03887.0002.NPUS00	1758
27194	7590	02/25/2004	EXAMINER	
HOWREY SIMON ARNOLD & WHITE, LLP			SHUKLA, RAM R	
BOX 34			ART UNIT	
301 RAVENSWOOD AVE.			PAPER NUMBER	
MENLO PARK, CA 94025			1632	

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/051,956

Applicant(s)

MOBRAATEN ET AL.

Examiner

Ram R. Shukla

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 05 December 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) 14-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All   b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 7-8-02.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

1. Applicant's election without traverse of the invention of group I, claims 1-13 in Paper filed 12-05-2003 is acknowledged.
2. Claims 14-28 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper filed 12-05-2003.
3. Claims 1-13 directed to a method of producing non-human mammal is under consideration.

### ***Information Disclosure Statement***

4. The specification is objected because pages 17-21 of the specification contain a listing of references.

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

5. No priority has been claimed.

### ***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakagata et al (Biology of Reproduction 57:1050-1055, 1997) in view of Bertrand et al (Human Reproduction 10:1189-1193, 1995), Mordel et al (Journal of Assisted Reproduction and Genetics 9:128-132, 1992) and Lubart et al (US 6,379,939, 4-30-2002).

Nakagata et al teaches a need for developing methods for maintaining established lines of transgenic mouse (see the introduction section on page 1050 and the discussion on page 1053). The art also teaches freezing of mouse spermatozoa after collection and using these for fertilization. The art also teaches partial zona dissection for improving fertilization of oocytes by cryopreserved sperms (see the last paragraph of the introduction). The art also teaches super ovulation by eCG injection, collection of oocytes, their treatment with HTF medium and hyaluronidase solution, procedure for partial removal of zona pellucida (see the methods section). The art does not teach reducing circumferential thickness of the zona pellucida layer without removing it completely.

Bertrand et al teaches that importance of zona pellucida thickness in fertilization rate and that a thick zona pellucida forces the spermatozoa to travel further than through a standard zona pellucida and so the spermatozoa are more likely to fail before reaching the cytoplasm. The art also discusses results from other investigators that patients with thin zona pellucida have more chance of becoming pregnant than those with thicker zona pellucida and that if the variation

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of the zona pellucida thickness for each embryo is >25%, the implantation rate increases (see the discussion on page 1192, left column).

Mordel et al teaches enhancement of in vitro fertilization of mouse oocytes by partial zona pellucida digestion by treating the oocytes with a Ham's F10 solution containing Pronase E and protease type XXV) (see the methods section). These authors reported uniform dissolution of zona pellucida and reduction in its thickness is a safe process and increases fertilization (see the discussion section). This art also teaches treatment of the oocytes with acid Tyrode's solution, which also significantly increases fertilization rate. The art further teaches that it is possible to enhance fertilization rate at concentration similar to those existing in the fallopian tube with a technically simple and less aggressive procedure.

In addition, arts at the time of the instant invention routinely used treatment of the oocyte with Tyrode's solution, Hyaluronidase, Trypsin etc. to remove cumulus and zona pellucida (e.g. see column 2, lines 43-58 in US 6,379,939).

At the time of the invention, it would have been obvious to an artisan of ordinary skill to modify the method of Nakagata et al and treat the oocytes with Tyrode's solution, Protease solution, hyaluronidase solution for partially digesting the zona pellucida before fertilization with a cryopreserved spermatozoa and transplant the fertilized oocytes in a female non-human mammal to produce offspring for maintaining lines of animals with a reasonable expectation of success. An artisan of skill would have been motivated to treat the oocytes with zona pellucida thinning solutions or other methods because this would have increased the fertilization rate and because the cryopreserved spermatozoa have lower fertilization rate compared to non-preserved spermatozoa (see Bertrand et al and Mordel et al).

8. No claim is allowed.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (571) 272-0735 . The examiner can normally be reached on Monday through Friday

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from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (571) 272-0734. The fax phone number for TC 1600 is (703) 703-872-9306. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the William Phillips whose telephone number is (571) 272-0548.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ram R. Shukla, Ph.D.  
Primary Examiner  
Art Unit 1632

  
**RAM R. SHUKLA, PH.D.**  
**PRIMARY EXAMINER**